TAB 17

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

IN RE NATIONAL PRESCRIPTION OPIATE LITIGATION

This document relates to:

Case No. 1:17-op-45053-DAP (S.D. W.Va.)
and
Case No. 1:17-op-45054 (S.D. W.Va.)

CABELL COUNTY COMMISSION and CITY OF HUNTINGTON, WEST VIRGINIA,

Plaintiff,

PURDUE PHARMA L.P., PURDUE PHARMA INC., THE PURDUE FREDERICK COMPANY, INC., RHODES PHARMACEUTICALS L.P., RHODES TECHNOLOGIES, INC., RICHARD S. SACKLER, M.D., KATHE A. SACKLER, JONATHAN D. SACKLER, MORTIMER D.A. SACKLER, ILENE SACKLER LEFCOURT, BEVERLY SACKLER, THERESA SACKLER, DAVID A. SACKLER, ALLERGAN PLC F/K/A ACTAVIS PLC F/K/A ALLERGAN INC., ALLERGAN FINANCE LLC F/K/A ACTAVIS INC. F/K/A WATSON PHARMACEUTICALS, INC., ALLERGAN SALES, LLC, ALLERGAN USA, INC., WATSON LABORATORIES, INC., WARNER CHILCOTT COMPANY, LLC, ACTAVIS PHARMA, INC. F/K/A WATSON PHARMA, INC., ACTAVIS SOUTH ATLANTIC LLC, ACTAVIS ELIZABETH LLC, ACTAVIS MID ATLANTIC LLC, ACTAVIS TOTOWA LLC, ACTAVIS LLC, ACTAVIS KADIAN LLC, ACTAVIS LABORATORIES UT, INC., ACTAVIS LABORATORIES FL, INC., JOHNSON & JOHNSON, JANSSEN

MDL No. 2804

Case No. 17-md-2804

Judge Dan Aaron Polster

CORRECTED JOINT AND THIRD AMENDED COMPLAINT

DEMAND FOR JURY TRIAL

PHARMACEUTICALS, INC., NORAMCO, INC., ORTHO-MCNEIL-JANSSEN PHARMACEUTICALS, INC. N/K/A JANSSEN PHARMACEUTICALS, INC., JANSSEN PHARMACEUTICA, INC. N/K/A JANSSEN PHARMACEUTICALS, INC., ENDO HEALTH SOLUTIONS INC., ENDO PHARMACEUTICALS, INC., PAR PHARMACEUTICAL, INC., PAR PHARMACEUTICAL COMPANIES, INC. F/K/A PAR PHARMACEUTICAL HOLDINGS, INC., TEVA PHARMACEUTICAL INDUSTRIES LTD., TEVA PHARMACEUTICALS USA, INC., CEPHALON, INC., MALLINCKRODT PLC, MALLINCKRODT LLC, SPECGX LLC, KVK-TECH, INC., AMNEAL PHARMACEUTICALS, LLC, AMNEAL PHARMACEUTICALS, INC., IMPAX LABORATORIES, LLC, AMNEAL PHARMACEUTICALS OF NEW YORK LLC, AMERISOURCEBERGEN DRUG CORPORATION, CARDINAL HEALTH, INC., MCKESSON CORPORATION, CVS HEALTH CORPORATION, CVS INDIANA L.L.C., CVS RX SERVICES, INC., CVS TENNESSEE DISTRIBUTION, L.L.C., CVS PHARMACY, INC., WEST VIRGINIA CVS PHARMACY, LLC, RITE AID CORPORATION, RITE AID OF MARYLAND, INC. D/B/A RITE AID MID-ATLANTIC CUSTOMER SUPPORT CENTER, INC., RITE AID OF WEST VIRGINIA, INC., WALGREENS BOOTS ALLIANCE, INC., WALGREEN EASTERN CO., INC., WALGREEN CO., H. D. SMITH WHOLESALE DRUG CO., KROGER LIMITED PARTNERSHIP I, KROGER LIMITED PARTNERSHIP II, WALMART INC, WAL-MART STORES EAST D/B/A WAL-MART PHARMACY WAREHOUSE #46, WAL-MART PHARMACY WAREHOUSE #45, WAL-MART PHARMACY WAREHOUSE, EXPRESS SCRIPTS HOLDING COMPANY, EXPRESS SCRIPTS, INC., CAREMARK RX, LLC,

OPTUM, INC., OPTUMRX INC.,
TASMANIAN ALKALOIDS PTY. LTD.

Defendants.

14. The City of Huntington and Cabell County are, by now, well-known for being situated at ground zero of the opioid epidemic sweeping the nation

15. This epidemic has been fueled and sustained by those involved in the supply chain of opioids, including manufacturers, distributors, pharmacies, and pharmacy benefit managers (together, "Defendants"), who (1) engineered a dramatic shift in how and when opioids are prescribed by the medical community and used by patients and (2) failed to maintain effective controls over the distribution of prescription opioids, by – among other things – selling and distributing far greater quantities of prescription opioids than they know could be necessary for legitimate medical uses, while failing to report, and to take steps to halt suspicious orders when they were identified.

South Atlantic LLC, Actavis Elizabeth LLC, Actavis Mid Atlantic LLC, Actavis Totowa LLC, Actavis Kadian LLC, Actavis Laboratories UT, Inc., Actavis Laboratories FL, Inc., , KVK-Tech, Inc., Amneal Pharmaceuticals LLC, Amneal Pharmaceuticals, Inc., Amneal Pharmaceuticals of New York LLC, Impax Laboratories, LLC, CVS Pharmacy, Inc., CVS Indiana L.L.C., CVS Rx Services, Inc., CVS Tennessee Distribution, L.L.C., West Virginia CVS Pharmacy, LLC, Rite Aid Of West Virginia, Inc., Walgreen Co., Express Scripts Holding Company, Express Scripts, Inc., Caremark Rx, LLC, CVS Health Corporation, Optum, Inc., OptumRx Inc., Tasmanian Alkaloids Pty. Ltd.

- Subsequent to the filing of its Second Amended Complaint, on July 6, 2018, Plaintiff Cabell County dismissed Rite Aid Corporation without prejudice.
- Subsequent to the filing of its Second Amended Complaint, on July 16, 2018, Plaintiff Cabell County:
  - i. Dismissed CVS Health Corporation without prejudice
  - ii. Dismissed Walgreens Boot Alliance, Inc., without prejudice
  - iii. Substituted parties CVS Tennessee Distribution, LLC, CVS Indiana LLC, and CVS RX Services, Inc.
- CVS Indiana LLC was previously named in the City of Huntington's Second Amended Complaint.

- The following were named as Defendants in the Second Amended Complaint, but are no longer named in the Third Amended Complaint: Insys.

8. KVK Tech

119. Defendant **KVK-TECH, INC**. is a privately held Pennsylvania corporation with its principal place of business in Pennsylvania. KVK-Tech, Inc.is a manufacturer of generic prescription opioids, including many Schedule II controlled substances such as Oxycodone and Hydrocodone.

120. KVK-Tech, Inc. has engaged in the manufacture, promotion, distribution, and sale of the generic prescription opioid drugs sold throughout the country, including into West Virginia and Cabell County.

9. Amneal Pharmaceuticals

121. Defendant **AMNEAL PHARMACEUTICALS LLC** is a Delaware limited liability company with its principal place of business in Bridgewater, New Jersey. Impax laboratories, LLC, formerly known as Impax Laboratories, Inc., is a Delaware limited liability company with its principle place of business in Bridgewater, New Jersey. Upon information and belief, in May 2018, Impax laboratories, Inc. merged with and into Amneal pharmaceuticals LLC to form Defendant, Amneal Pharmaceuticals, Inc., a Delaware Corporation with its principal place of business in Bridgewater, New Jersey. Defendant Amneal Pharmaceuticals of New York LLC is a Delaware limited liability company with its principal place of business in Hauppauge, New York. Amneal Pharmaceuticals, Inc., Amneal Pharmaceuticals LLC, Amneal Pharmaceuticals of New York LLC, and Impax Laboratories, LLC are collectively referred to as “Amneal.” Amneal manufactures, promotes, distributes and/or sells opioids nationally and in Cabell County and the City of Huntington.

deceptively and illegally in order to significantly increase sales and generate billions of dollars in revenue for Purdue's private owners, the Sackler family.

314. Purdue's strategies were quickly joined by other manufacturers, including Endo Health Solutions Inc.; Endo Pharmaceuticals, Inc.; Par Pharmaceutical, Inc.; Par Pharmaceutical Companies, Inc. f/k/a Par Pharmaceutical Holdings, Inc.; Janssen Pharmaceuticals, Inc.; Ortho-McNeil-Janssen Pharmaceuticals, Inc. n/k/a Janssen Pharmaceuticals, Inc.; Janssen Pharmaceutica, Inc. n/k/a Janssen Pharmaceuticals, Inc.; Johnson & Johnson; Noramco, Inc.; Teva Pharmaceutical Industries, Ltd.; Teva Pharmaceuticals USA, Inc.; Cephalon, Inc.; Mallinckrodt PLC; Mallinckrodt LLC; SpecGx LLC, Amneal, and KVK Tech (collectively the "Marketing Defendants").

315. Marketing Defendants manufacture, market, sell, and distribute branded and/or generic prescription opioid pain medications. Some of the relevant brand-name drugs include OxyContin, Butrans, Hysingla ER, Actiq, Fentora, Opana/Opana ER, Percodan, Percocet, Zydone, Nucynta/Nucynta ER, Duragesic, Exalgo, and Xartemis XR. The Marketing Defendants used misrepresentations regarding the risks and benefits of opioids to enable the widespread prescribing of opioids for common, chronic pain conditions like low back pain, arthritis, and headaches.[73]

316. Prescription opioids are narcotics. They are derived from and possess properties similar to opium and heroin, and they are regulated as controlled substances. While opioids can dampen the perception of pain, they also can create an addictive, euphoric high. At higher doses, they can slow the user's breathing, causing potentially fatal respiratory depression. Most patients receiving more than a few weeks of opioid therapy will experience withdrawal symptoms if opioid use is delayed or discontinued —including severe anxiety, nausea, headaches, tremors, delirium,

[73] Consistent with the commonly accepted medical usage, the term "chronic pain" as used herein refers to non-cancer pain lasting three months or longer.

and pain—which are often prolonged. When using opioids continuously, patients grow tolerant to their analgesic effects (i.e. to relief of pain)—requiring progressively higher doses and increasing the risks of withdrawal, addiction, and overdose.

317. Because the medical community recognized these dangers, they originally used opioids cautiously and sparingly, typically only for short-term acute pain—where brief use limited the need for escalating doses and the risk of addiction—or for palliative (end-of-life) care. Consequently, the market for prescription opioids was sharply constrained.

318. As Purdue developed OxyContin in the mid-1990s, it knew that to expand its market and profits, it needed to change the perception of opioids to permit and encourage the use of opioids long-term for widespread chronic conditions like back pain, migraines, and arthritis. Purdue, joined by the other Marketing Defendants began to promote opioids generally, and their own opioids in particular, as safe, effective, and appropriate for even long-term use for routine pain conditions. As part of this strategy, Defendants misrepresented the risk of addiction for pain patients as modest, manageable, and outweighed by the benefits of opioid use.

319. The Marketing Defendants' scheme was resoundingly successful. Chronic opioid therapy—the prescribing of opioids long-term to treat chronic pain—has become a commonplace, and often first-line, treatment. Marketing Defendants' deceptive marketing caused prescribing not only of their opioids, but of opioids as a class, to skyrocket. According to the CDC opioid prescriptions, as measured by number of prescriptions and morphine milligram equivalent ("MME") per person, tripled from 1999 to 2015. In 2015, on an average day, more than 650,000 opioid prescriptions were dispensed in the U.S. While previously a small minority of opioid sales, today between 80% and 90% of opioids (measured by weight) used are for chronic pain.

e. API volume growth linked to generics of branded drugs, new delivery systems & abuse prevention claims.

368. Noramco steadily gained in the U.S. market share reporting in 2014 alone that U.S. Sales of $94MM for Oxycodone and $52MM for Hydrocodone. In five years, from 2006 – 2011 their API volume growth doubled and continue climbing for the need for new capacity in 2015. Janssen's fully integrated supply chain provided security for continued growth.

369. Janssen fueled the opioid epidemic by providing a more potent poppy that could provide greater supply and/or profits. But, because of Noramco and Tasmanian Alkaloids, Janssen had an incentive to fraudulently market opioids with other Marketing Defendants as Janssen profited not only from its own opioid products, but from the sale of its API to other manufacturers.

370. Ironically, Janssen also profited from the rising addictions and abuse of opioids by suppling API for use in Naloxone for overdose and abuse, and in Naltrexone and Buprenorphine for opioid addiction.

371. By adding additional opioids or expanding the use of their existing opioid products, the other Marketing Defendants took advantage of the market created by Purdue's aggressive promotion of OxyContin and reaped enormous profits. For example, Opana ER alone generated more than $1 billion in revenue for Endo in 2010 and again in 2013. Janssen also passed the $1 billion mark in sales of Duragesic in 2009.

E. The Marketing Defendants' Multi-Pronged Scheme to Change Prescriber Habits and Public Perception and Increase Demand for Opioids

372. Until the mid-1990s, opioids were widely thought to be too addictive for use for chronic pain conditions, which would require long-term use of the drugs at increasingly high doses. For these conditions, the risks of addiction and other side effects outweighed any benefit from the drugs. Over the last two decades, Marketing Defendants turned that consensus on its head by

designing and implementing a sophisticated and deceptive market strategy that, among other things, falsely denied the risk of addiction and overstated the benefits of using opioids long-term.

373. Lacking legitimate scientific research to support their claims, Marketing Defendants turned to the marketing techniques first pioneered by Arthur Sackler to create a series of misperceptions in the medical community and ultimately reverse the long-settled understanding of the relative risks and benefits of opioids.

374. Through marketing that was as pervasive as it was deceptive, Marketing Defendants convinced health care providers both that the risks of long-term opioid use were overblown and that the benefits, in reduced pain and improved function and quality of life, were proven. Purdue, for example, promoted the concept that pain was undertreated, that opioids could not be abused, that the rate of addiction to opioids was less than 1%, that "old views" of opioid addiction were untrue, and that "appropriate patients" would not become addicted.

375. The result was that by the mid-2000s, the medical community had abandoned its prior caution, and opioids were entrenched as an appropriate—and often the first—treatment for chronic pain conditions. Marketing Defendants not only marketed opioids for chronic pain conditions, but also targeted primary care physicians (along with nurse practitioners and physician assistants), [90] who were most likely to see patients with chronic pain conditions and least likely to have the training and experience to evaluate Marketing Defendants' marketing claims.

376. Marketing Defendants' deceptive marketing created a cadre of doctors who looked for pain and treated it with opioids, which created an even broader cohort of patients who expected

[90] For example, in 2013, Purdue sought to identify Key Opinion Leaders ("KOLs") to reach non-physician prescribers, including for a program to educate nurses about opioids. By 2015, nurse practitioners and physician assistants were responsible for over 800 million prescriptions and constituted Purdue's largest growth area.

and received opioids. This laid the groundwork for today's epidemic of opioid addiction, injury, and death.

377. The Marketing Defendants promoted, and profited from, their misrepresentations about the risks and benefits of opioids for chronic pain even though they knew that their marketing was false and misleading. The history of opioids, as well as research and clinical experience over the last 20 years, established that opioids were highly addictive and responsible for a long list of very serious adverse outcomes. The FDA and other regulators warned Marketing Defendants of these risks. The Marketing Defendants had access to scientific studies, detailed prescription data, and reports of adverse events, including reports of addiction, hospitalization, and deaths—all of which made clear the harms from long-term opioid use and that patients are suffering from addiction, overdoses, and death in alarming numbers. More recently, the FDA and CDC issued pronouncements based on existing medical evidence that conclusively expose the known falsity of these Defendants' misrepresentations.

378. The marketing scheme to increase opioid prescriptions centered around nine categories of misrepresentations, which are discussed in detail below. The Marketing Defendants disseminated these misrepresentations through various channels, including through advertising, sales representatives, purportedly independent organizations these defendants funded and controlled, "Front Groups," so-called industry "Key Opinion Leaders," and Continuing Medical Education ("CME") programs discussed subsequently below.

1. The Marketing Defendants Promoted Multiple Falsehoods About Opioids

379. Marketing Defendants spent hundreds of millions of dollars on promotional activities and materials, including advertising, and websites that falsely denied or trivialized the risk of addiction and overstated the benefits of opioids. They also relied upon unsupported and

misleading information derived from seminars, treatment guidelines, and other publications and programs by patient advocacy groups, professional associations, and physicians that seemed independent and therefore credible, but were actually funded and controlled by Marketing Defendants.

380. For example, Purdue recruited and paid respected health care professionals as "speakers" who presented Purdue-approved programs to other prescribers at lunch and dinner events. From 1996 to 2001, Purdue held more than 40 national conferences and more than 5,000 physicians, pharmacist, and nurses attended these speaker conferences. In addition to speaker programs, Purdue targeted doctors with "educational" programing and funded more than 20,000 pain-related educational programs through direct sponsorship or financial grants by July 2002.

381. Marketing Defendants also used "key opinion leaders" ("KOLs")—experts in the field who were especially influential because of their reputations and seeming objectivity—to deliver paid talks and continuing medical education programs (or "CMEs") that provided information about treating pain and the risks, benefits, and use of opioids. These KOLs received substantial funding and research grants from the Marketing Defendants, and the CMEs were often sponsored by Defendants—giving them considerable influence over the messenger, the message, and the distribution of the program. Only doctors supportive of the use and safety of opioids for chronic pain received these funding and speaking opportunities, which were not only lucrative, but also helped doctors build their reputations and bodies of work. One notable KOL, Dr. Russell Portenoy, subsequently acknowledged that he gave lectures on opioids that reflected "misinformation" and were "clearly the wrong thing to do."

382. In addition to talks and CMEs, these KOLs served on the boards of patient advocacy groups and professional associations, such as the American Pain Foundation and the American

Pain Society, which also took money directly from Marketing Defendants in an organized effort to exert greater influence because of their seeming independence. According to a report issued by the U.S. Senate Homeland Security & Governmental Affairs Committee, Ranking Member's Office, "many patient advocacy organizations and professional societies focusing on opioids policy have promoted messages and policies favorable to opioid use while receiving millions of dollars in payments from opioid manufacturers. Through criticism of government prescribing guidelines, minimization of opioid addiction risk, and other efforts, ostensibly neutral advocacy organizations have often supported industry interests at the expense of their own constituencies."[91] These "front groups" for the opioid industry put out unbranded patient education materials and treatment guidelines that supported the use of opioids for chronic pain, overstated their benefits, and understated their risks. In many instances, Marketing Defendants distributed these publications to prescribers, including, upon information and belief, prescribers in the City, or posted them on their websites.

383. These third-party, unbranded materials were not reviewed or approved by the FDA. The FDA does not regulate all conduct engaged in by these Defendants. Marketing for chronic pain is not specifically approved. Medication labels do not address the use of opioids in treating specific conditions such as lower back pain, headaches, or fibromyalgia—three conditions for which opioids are not effective, but for which these Defendants marketed their drugs. Nor do the labels approve of the concept of "pseudoaddiction" or the technique of suggesting that abuse deterrent formulations are safer. In addition, though labels contain warnings about addiction, they do not quantify the severity of the risk. Marketing Defendants' asserted in branded and unbranded

[91] U.S. S. Homeland Sec. & Governmental Aff. Comm., Ranking Members' Office, *Fueling an Epidemic*, Feb. 12, 2018, https://www.hsdl.org/?abstract&did=808171 at 3 (hereinafter, "*Fueling an Epidemic*").

marketing that screening, abuse deterrent formulations, or urinalysis could adequately manage the risk of developing an addiction without evidence to support these claims.

384. The Marketing Defendants' misrepresentations generally fall into the following nine categories:

1. The risk of addiction from chronic opioid therapy is low
2. Signs of addictive behavior are "pseudoaddiction," requiring more opioids
3. To the extent there is a risk of addiction, it can be easily identified and managed
4. Opioid withdrawal can be avoided by tapering
5. Long-term opioid use improves functioning
6. Opioid doses can be increased without limit or greater risks
7. Alternative forms of pain relief pose greater risks than opioids
8. OxyContin provides twelve hours of pain relief
9. New formulations of certain opioids successfully deter abuse

385. Each of these propositions was false. The Marketing Defendants knew this, but they nonetheless set out to convince physicians, patients, and the public at large of the truth of each of these propositions in order to expand the market for their opioids.

386. The categories of misrepresentations are offered to organize the numerous statements the Marketing Defendants made and to explain their role in the overall marketing effort, not as a checklist for assessing each Marketing Defendant's liability. While each Marketing Defendant deceptively promoted their opioids specifically, and, together with other Marketing Defendants, opioids generally, not every Marketing Defendant propagated (or needed to propagate) each misrepresentation. Each Marketing Defendant's conduct, and each misrepresentation, contributed to an overall narrative that aimed to—and did—mislead doctors,

patients, and payors about the risk and benefits of opioids. While this Complaint endeavors to document examples of each Marketing Defendant's misrepresentations and the manner in which they were disseminated, they are just that—examples. The Complaint is not, especially prior to discovery, an exhaustive catalog of the nature and manner of each deceptive statement by each Marketing Defendant.

387. Upon information and belief, all of the messages described below were disseminated to prescribers and patients in Plaintiffs' communities.

Falsehood #1: The risk of addiction from chronic opioid therapy is low

388. To convince prescribers and patients that opioids are safe, Marketing Defendants deceptively represented that the risk of abuse and addiction is modest and manageable and limited to illegitimate patients, not those with genuine pain. This created the dangerously misleading impressions that: (1) patients receiving opioid prescriptions for chronic pain would not become addicted, (2) patients at greatest risk of addiction could be identified, and (3) all other patients could safely be prescribed opioids.

389. Marketing Defendants undermined evidence that opioids are addictive by suggesting or stating that the risk of addiction is limited to high-risk patients. These Defendants also minimized the difficulty of withdrawal in their marketing material and promotional programs. For example, a 2011 non-credit educational program sponsored by Endo, entitled Persistent Pain in the Older Adult, claimed that withdrawal symptoms, which make it difficult for patients to stop using opioids, could be avoided by simply tapering a patient's opioid dose over ten days. However, this claim is at odds with the experience of patients addicted to opioids. Most patients who are dependent upon or addicted to opioids will experience withdrawal, characterized by intense physical and psychological effects, including anxiety, nausea, headaches, and delirium, among

others. This painful and arduous struggle to terminate use can leave many patients unwilling or unable to give up opioids and heightens the risk of addiction.

i. Purdue's misrepresentations regarding addiction risk

390. When it launched OxyContin, Purdue knew it would need data to overcome decades of wariness regarding opioid use. It needed some sort of research to back up its messaging. But Purdue had not conducted any studies about abuse potential or addiction risk as part of its application for FDA approval for OxyContin. Purdue (and, later, the other Defendants) found this "research" in the form of a one-paragraph letter to the editor published in the *New England Journal of Medicine* (NEJM) in 1980.

391. This letter, by Dr. Hershel Jick and Jane Porter, declared the incidence of addiction "rare" for patients treated with opioids.[92] They had analyzed a database of hospitalized patients who were given opioids in a controlled setting to ease suffering from acute pain. Porter and Jick considered a patient not addicted if there was no sign of addiction noted in patients' records.

[92] Jane Porter and Herschel Jick, MD, *Addiction Rare in Patients Treated with Narcotics*, 302(2) N Engl J Med. 123 (Jan. 10, 1980), http://www.nejm.org/doi/pdf/10.1056/NEJM198001103020221.

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug Surveillance Program
Boston University Medical Center
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1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

392. As Dr. Jick explained to a journalist years later, he submitted the statistics to NEJM as a letter because the data were not robust enough to be published as a study.[93]

393. Purdue nonetheless began repeatedly citing this letter in promotional and educational materials as evidence of the low risk of addiction, while failing to disclose that its source was a letter to the editor, not a peer-reviewed paper.[94] Citation of the letter, which was largely ignored for more than a decade, significantly increased after the introduction of OxyContin. While first Purdue and then other Marketing Defendants used it to assert that their opioids were not addictive, "that's not in any shape or form what we suggested in our letter," according to Dr. Jick.

394. Purdue specifically used the Porter and Jick letter in its 1998 promotional video, "I got my life back," in which Dr. Alan Spanos says, "In fact, the rate of addiction amongst pain patients who are treated by doctors *is much less than 1%*."[95] Purdue trained its sales

[93] Meier at 174.
[94] J. Porter & H. Jick, Addiction Rare in Patients Treated with Narcotics, 302(2) New. Eng. J. Med. 123 (1980).
[95] Our Amazing World, *Purdue Pharma OxyContin Commercial*, https://www.youtube.com/watch?v=Er78Dj5hyeI

representatives to tell prescribers that fewer than 1% of patients who took OxyContin became addicted. (In 1999, a Purdue-funded study of patients who used OxyContin for headaches found that the addiction rate was thirteen per cent.)"[96]

395. Other Defendants relied on and disseminated the same distorted messaging. The enormous impact of Defendants' misleading amplification of this letter was well documented in another letter published in the NEJM on June 1, 2017, describing the way the one-paragraph 1980 letter had been irresponsibly cited and in some cases "grossly misrepresented." In particular, the authors of this letter explained:

> [W]e found that a five-sentence letter published in the *Journal* in 1980 was heavily and uncritically cited as evidence that addiction was rare with long-term opioid therapy. We believe that this citation pattern contributed to the North American opioid crisis by helping to shape a narrative that allayed prescribers' concerns about the risk of addiction associated with long-term opioid therapy . . .[97]

396. "It's difficult to overstate the role of this letter," said Dr. David Juurlink of the University of Toronto, who led the analysis. "It was the key bit of literature that helped the opiate manufacturers convince front-line doctors that addiction is not a concern."[98]

397. Alongside its use of the Porter and Jick letter, Purdue also crafted its own materials and spread its deceptive message through numerous additional channels. In its 1996 press release announcing the release of OxyContin, for example, Purdue declared, "The fear of addiction is exaggerated."[99]

(last visited Jan. 31, 2018) (emphasis added).

[96] Patrick Radden Keefe, *The Family That Built an Empire of Pain*, New Yorker (Oct. 30, 2017).

[97] Pamela T.M. Leung, B.Sc. Pharm., Erin M. Macdonald, M.Sc., Matthew B. Stanbrook, M.D., Ph.D., Irfan Al Dhalla, M.D., David N. Juurlink, M.D., Ph.D., *A 1980 Letter on the Risk of Opioid Addiction*, 376 N Engl J Med 2194-95 (June 1, 2017), http://www.nejm.org/doi/full/10.1056/NEJMc1700150#t=article.

[98] *Painful words: How a 1980 letter fueled the opioid epidemic*, STAT (May 31, 2017), https://www.statnews.com/2017/05/31/opioid-epidemic-nejm-letter/.

[99] Press Release, OxyContin, *New Hope for Millions of Americans Suffering from Persistent Pain: Long-Acting OxyContin Tablets Now Available to Relieve Pain* (May 31, 1996, 3:47pm), http://documents.latimes.com/oxycontin-press-release-1996/.

398. At a hearing before the House of Representatives' Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce in August 2001, Purdue emphasized "legitimate" treatment, dismissing cases of overdose and death as something that would not befall "legitimate" patients: "Virtually all of these reports involve people who are abusing the medication, not patients with legitimate medical needs under the treatment of a healthcare professional."[100]

399. Purdue spun this baseless "legitimate use" distinction out even further in a patient brochure about OxyContin, called "A Guide to Your New Pain Medicine and How to Become a Partner Against Pain." In response to the question "Aren't opioid pain medications like OxyContin Tablets 'addicting'?," Purdue claimed that there was no need to worry about addiction if taking opioids for legitimate, "medical" purposes:

> Drug addiction means using a drug to get "high" rather than to relieve pain. You are taking opioid pain medication for medical purposes. The medical purposes are clear and the effects are beneficial, not harmful.

400. Sales representatives marketed OxyContin as a product "'to start with and to stay with.'" [101] Sales representatives also received training in overcoming doctors' concerns about addiction with talking points they knew to be untrue about the drug's abuse potential. One of Purdue's early training memos compared doctor visits to "firing at a target," declaring that "[a]s you prepare to fire your 'message,' you need to know where to aim and what you want to hit!" [102]

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[100] *OxyContin: Its Use and Abuse: Hearing Before the H. Subcomm. on Oversight and Investigations of the Comm. on Energy and Commerce*, 107th Cong. 1 (Aug. 28, 2001) (statement of Michael Friedman, Executive Vice President, Chief Operating Officer, Purdue Pharma, L.P.), https://www.gpo.gov/fdsys/pkg/CHRG-107hhrg75754/html/CHRG-107hhrg75754.htm.

[101] Keefe, *Empire Of Pain.*

[102] Meier, *Pain Killer*, at 102.

According to the memo, the target is physician resistance based on concern about addiction: "The physician wants pain relief for these patients without addicting them to an opioid." [103]

401. Purdue, through its unbranded website *Partners Against Pain*, [104] stated the following: "Current Myth: Opioid addiction (psychological dependence) is an important clinical problem in patients with moderate to severe pain treated with opioids. Fact: Fears about psychological dependence are exaggerated when treating appropriate pain patients with opioids." "Addiction risk also appears to be low when opioids are dosed properly for chronic, noncancer pain."

402. Former sales representative Steven May, who worked for Purdue from 1999 to 2005, explained to a journalist how he and his coworkers were trained to overcome doctors' objections to prescribing opioids. The most common objection he heard about prescribing OxyContin was that "it's just too addictive."[105] May and his coworkers were trained to "refocus" doctors on "legitimate" pain patients, and to represent that "legitimate" patients would not become addicted. In addition, they were trained to say that the 12-hour dosing made the extended-release opioids less "habit-forming" than painkillers than need to be taken every four hours.

403. According to interviews with prescribers and former Purdue sales representatives, Purdue has continued to distort or omit the risk of addiction while failing to correct its earlier

[103] *Id*.

[104] *Partners Against Pain* consists of both a website, styled as an "advocacy community" for better pain care, and a set of medical education resources distributed to prescribers by sales representatives. It has existed since at least the early 2000s and has been a vehicle for Purdue to downplay the risks of addiction from long-term opioid use. One early pamphlet, for example, answered concerns about OxyContin's addictiveness by claiming: "Drug addiction means using a drug to get 'high' rather than to relieve pain. You are taking opioid pain medication for medical purposes. The medical purposes are clear and the effects are beneficial, not harmful."

[105] David Remnick, *How OxyContin Was Sold to the Masses* (Steven May interview with Patrick Radden Keefe), The New Yorker (Oct. 27, 2017), https://www.newyorker.com/podcast/the-new-yorker-radio-hour/how-oxycontin-was-sold-to-the-masses.

misrepresentations, leaving many doctors with the false impression that pain patients will only rarely become addicted to opioids.

404. With regard to addiction, Purdue's label for OxyContin has not sufficiently disclosed the true risks to, and experiences of, its patients. Until 2014, the OxyContin label stated in a black-box warning that opioids have "abuse potential" and that the "risk of abuse is increased in patients with a personal or family history of substance abuse."

405. However, the FDA made clear to Purdue as early as 2001 that the disclosures in its OxyContin label were insufficient. Senior FDA officials met with Purdue on April 23, 2001, to "provide comments and suggestions on a Risk Management program for OxyContin. "Among other issues, the FDA noted that Purdue should add a black-box warning for overdose, abuse, and death to OxyContin's label. Purdue acknowledged that it was aware of abuse of OxyContin orally (without tampering), as well as by snorting or injecting. It was not, the FDA explained, a matter of changing a few words in OxyContin's label; Dr. Cynthia McCormick, then director of the FDA division overseeing pain medication, declared that "'major overhaul is my message.' The prescribing of OxyContin is creeping into a whole population of people where it doesn't belong. Just rewriting the abuse and dependence section won't help much, that part of the insert is not a pivot point."

406. Another FDA participant asked that Purdue "refocus our promotional materials and make the risks of abuse and diversion more prominent." In short, the FDA advised Purdue "that the information put in the label back at the time of product approval did not adequately address the risks associated with this product and this needs to be corrected."

407. In 2001, Purdue revised the indication and warnings for OxyContin, but did not go nearly as far as the FDA recommended or the known risks of the product demanded. In the United

States, Purdue ceased distributing the 160 mg tablet of OxyContin. While Purdue agreed to "consider" changes to its label, it also expressed a reluctance to make significant changes not required for other prescription opioids. Dr. McCormick noted that the issues discussed at the meeting were specific to OxyContin and that, while the Agency would talk with Purdue's competitors, "'we have a problem here and now with OxyContin.' In due time other manufacturers will be contacted but the first problem is this product."

408. In the end, Purdue narrowed the recommended use of OxyContin to situations when "a continuous, around-the-clock analgesic is needed for an extended period of time" and added a warning that "[t]aking broken, chewed, or crushed OxyContin tablets" could lead to a "potentially fatal dose." However, Purdue did not, until 2014, change the label as the FDA suggested, to indicate that OxyContin should not be the first therapy, or even the first opioid, used, and did not disclose the incidence or risk of overdose and death even when OxyContin was not abused. Purdue announced the label changes in a letter to health care providers but did not, as the FDA suggested, issue "a Medguide for patients on the risks of overdose and the abuse of opioids as well as risks for use by others than those for whom it was prescribed" or undertake the recommended promotional effort to educate patients about the potentially fatal risks of OxyContin.

409. The FDA also informed Purdue what Purdue already knew, as noted above—that "there is a perception that oxycodone is safer than morphine." A representative from the FDA's Division of Drug Marketing, Advertising and Communications echoed this, calling for an "extensive educational effort to consumers and health care practitioners" to "correct a misconception that [OxyContin] is different than morphine." Upon information and belief, Purdue never undertook that effort.

410. Purdue also heavily promoted the Joint Commission on Accreditation of Healthcare Organization's Pain as a Fifth Vital Sign, which encouraged health care providers to ask about pain and, presumably, to treat it with opioids. Purdue obtained exclusive rights to distribute Pain as a Fifth Vital Sign, and made sure that this guide, intended initially for hospital patients, was widely disseminated. Front groups supported by Marketing Defendants, particularly the University of Wisconsin Pain and Policy Study Group (PPSG), proposed the concept of Pain as a Fifth Vital Sign, which the review committee of outside physicians charged with evaluating guidelines rejected precisely because of their concern that it would result in overuse of opioids and increased addiction and overdose. JACHO nonetheless adopted by guidelines, presumably at the behest of PPSG and its supporters.

ii. Endo's misrepresentations regarding addiction risk

411. Endo also falsely represented that addiction is rare in patients who are prescribed opioids.

412. Until April 2012, Endo's website for Opana, *www.opana.com*, stated that "[m]ost healthcare providers who treat patients with pain agree that patients treated with prolonged opioid medicines usually do not become addicted."

413. Upon information and belief, Endo improperly instructed its sales representatives to diminish and distort the risk of addiction associated with Opana ER. Endo's training materials for its sales representatives in 2011 also prompted sales representatives to answer "true" to the statement that addiction to opioids is not common.

414. One of the Front Groups with which Endo worked most closely was the American Pain Foundation ("APF"), described more fully below. Endo provided substantial assistance to, and exercised editorial control, over the deceptive and misleading messages that APF conveyed

through its National Initiative on Pain Control ("NIPC")[106] and its website *Painknowledge.com*, which claimed that "[p]eople who take opioids as prescribed usually do not become addicted."

415. Another Endo website, *PainAction.com*, stated: "Did you know? Most chronic pain patients do not become addicted to the opioid medications that are prescribed for them."

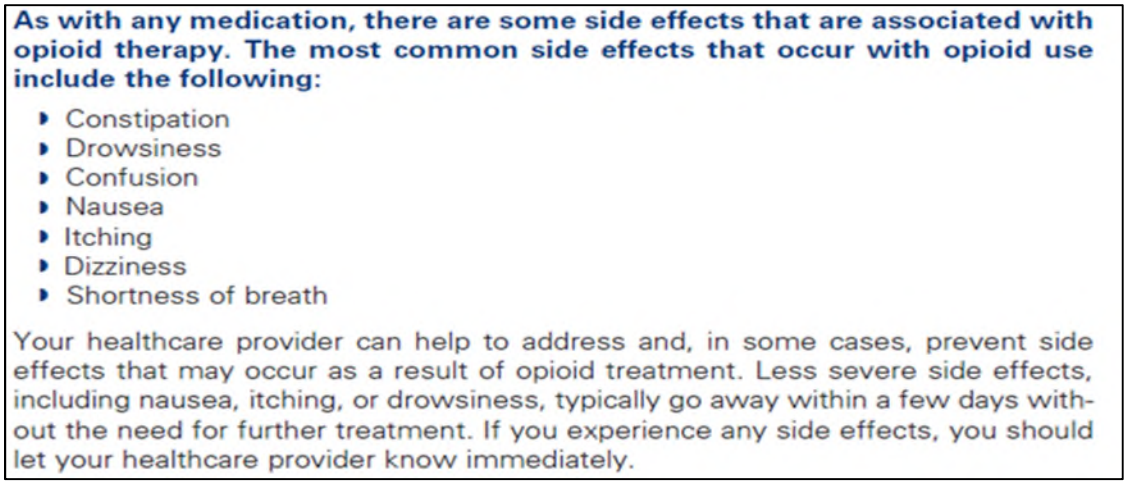
416. A brochure available on *Painknowledge.com* titled "*Pain: Opioid Facts*," Endo-sponsored NIPC stated that "people who have no history of drug abuse, including tobacco, and use their opioid medication as directed will probably not become addicted."[107] In numerous patient education pamphlets, Endo repeated this deceptive message.

- In a patient education pamphlet titled "*Understanding Your Pain: Taking Oral Opioid Analgesics*," Endo answers the hypothetical patient question—"What should I know about opioids and addiction?"—by focusing on explaining what addiction is ("a chronic brain disease") and is not ("Taking opioids for pain relief"). It goes on to explain that "[a]ddicts take opioids for other reasons, such as unbearable emotional problems. Taking opioids as prescribed for pain relief is not addiction." This publication is still available online.

417. An Endo publication, *Living with Someone with Chronic Pain*, stated, "Most health care providers who treat people with pain agree that most people do not develop an addiction problem." A similar statement appeared on the Endo website, www.opana.com, until at least April 2012.

418. In addition, a 2009 patient education publication, *Pain: Opioid Therapy*, funded by Endo and posted on *Painknowledge.com*, omitted addiction from the "common risks" of opioids, as shown below:

[106] Endo was one of the APF's biggest financial supporters, providing more than half of the $10 million APF received from opioid manufacturers during its lifespan. Endo was the sole funder of NIPC and selected APF to manage NIPC. Internal Endo documents indicate that Endo was responsible for NIPC curriculum development, web posting, and workshops, developed and reviewed NIPC content, and took a substantial role in distributing NIPC and APF materials. Endo projected that it would be able to reach tens of thousands of prescribers nationwide through the distribution of NIPC materials.



As with any medication, there are some side effects that are associated with opioid therapy. The most common side effects that occur with opioid use include the following:

- Constipation
- Drowsiness
- Confusion
- Nausea
- Itching
- Dizziness
- Shortness of breath

Your healthcare provider can help to address and, in some cases, prevent side effects that may occur as a result of opioid treatment. Less severe side effects, including nausea, itching, or drowsiness, typically go away within a few days without the need for further treatment. If you experience any side effects, you should let your healthcare provider know immediately.

iii. Janssen's misrepresentations regarding addiction risk

419. Janssen likewise misrepresented the addiction risk of opioids on its websites and print materials. One website, *Let's Talk Pain*, states, among other things, that "the stigma of drug addiction and abuse" associated with the use of opioids stemmed from a "lack of understanding about addiction." (Although Janssen described the website internally as an unbranded third-party program, it carried Janssen's trademark and copy approved by Janssen.)

420. The *Let's Talk Pain* website also perpetuated the concept of pseudoaddiction, associating patient behaviors such as "drug seeking," "clock watching," and "even illicit drug use or deception" with undertreated pain which can be resolved with "effective pain management." In August 2009, a "12 month review" of the *Let's Talk Pain* website manuscript confirmed that the website's contents included statements regarding pseudoaddiction and illustrated Janssen's control over the website and awareness of its contents.

421. A Janssen unbranded website, *PrescribeResponsibly.com*, states that concerns about opioid addiction are "overestimated" and that "true addiction occurs only in a small percentage of patients."[108]

[108] Keith Candiotti, M.D., *Use of Opioid Analgesics in Pain Management*, Prescribe Responsibly, http://www.prescriberesponsibly.com/articles/opioid-pain-management (last modified July 2, 2015).

422. Janssen reviewed, edited, approved, and distributed a patient education guide entitled *Finding Relief: Pain Management for Older Adults*, which, as seen below, described as "myth" the claim that opioids are addictive, and asserted as fact that "[m]any studies show that opioids are rarely addictive when used properly for the management of chronic pain." Until recently, this guide was still available online.

423. Janssen's website for Duragesic included a section addressing "Your Right to Pain Relief" and a hypothetical patient's fear that "I'm afraid I'll become a drug addict." The website's response: "Addiction is relatively rare when patients take opioids appropriately."

424. According to an internal marketing assessment, Janssen sales representatives were trained to emphasize that Nucynta ER had fewer side effects than other opioids, though, upon information and belief, this was an untrue and unsubstantiated superiority claim.

425. Janssen also conducted a research study on prescribers regarding the visual aids for the marketing of Nucynta ER. Doctors reportedly were interested that Nucynta was described as appropriate for patients at risk for addiction and to avoid addictive narcotics for young people. Additionally, doctors identified the advantages of Nucynta, which included that it was potentially less addicting than other opioids and had a lower street value.

426. Janssen also published a patient guide, *Patient Booklet Answers to Your Questions – Duragesic*, which stated that "Addiction is relatively rare when patients take opioids appropriately."

427. Janssen recognized that this misrepresentation was particularly important to payors, who had a "negative" reaction to covering an addictive drug for a chronic condition for which non-narcotic drugs were available.

iv. Cephalon's misrepresentations regarding addiction risk

428. Cephalon sponsored and facilitated the development of a guidebook, *Opioid Medications and REMS: A Patient's Guide*, which included claims that "patients without a history of abuse or a family history of abuse do not commonly become addicted to opioids." Similarly, Cephalon sponsored APF's *Treatment Options: A Guide for People Living with Pain* (2007), which taught that addiction is rare and limited to extreme cases of unauthorized dose escalations, obtaining opioids from multiple sources, or theft.

429. For example, a 2003 Cephalon-sponsored CME presentation titled *Pharmacologic Management of Breakthrough or Incident Pain*, posted on Medscape in February 2003, teaches:

> [C]hronic pain is often undertreated, particularly in the noncancer patient population. . . . The continued stigmatization of opioids and their prescription, coupled with often unfounded and self-imposed physician fear of dealing with the highly regulated distribution system for opioid analgesics, remains a barrier to effective pain management and must be addressed. Clinicians intimately involved with the treatment of patients with chronic pain recognize that the majority of suffering patients lack interest in substance abuse. In fact, patient fears of developing substance abuse behaviors such as addiction often lead to undertreatment of pain. The concern about patients with chronic pain becoming addicted to opioids during long-term opioid therapy may stem from confusion between physical dependence (tolerance) and psychological dependence (addiction) that manifests as drug abuse.[109]

[109] Michael J. Brennan, et al., Pharmacologic Management of Breakthrough or Incident Pain, Medscape, http://www.medscape.org/viewarticle/449803 (last visited Oct. 10, 2017).

430. An internal "educational" document claimed that "in patients without personal or family history of substance abuse, addiction resulting from exposure to opioid therapy is uncommon." The document continued, "Like patients, caregivers may need reassurance that few people using opioids for a legitimate medical reason become addicted to the drug, and that physical dependence to a drug is easily overcome through scheduled dosing decreases . . . " Upon information and belief, this Cephalon "learning module" was used to train sales representatives for their interactions with prescribers.

v. Actavis's misrepresentations regarding addiction risk

431. Through its "Learn More about customized pain control with Kadian" material, Actavis claimed that it is possible to become addicted to morphine-based drugs like Kadian, but that it is "less likely" to happen in those who "have never had an addiction problem." The piece goes on to advise that a need for a "dose adjustment" is the result of tolerance, and "not addiction."

432. Training for Actavis sales representatives deceptively minimizes the risk of addiction by: (i) attributing addiction to "predisposing factors" like family history of addiction or psychiatric disorders; (ii) repeatedly emphasizing the difference between substance dependence and substance abuse; and (iii) using the term pseudoaddiction, which, as described below, dismisses evidence of addiction as the undertreatment of pain and, dangerously, counsels doctors to respond to its signs with more opioids.

433. Actavis conducted a market study on takeaways from prescribers' interactions with Kadian sales representatives. The doctors had a strong recollection of the sales representatives' discussion of the low-abuse potential. Actavis' sales representatives' misstatements on the low-abuse potential was considered an important factor to doctors, and was most likely repeated and reinforced to their patients. Additionally, doctors reviewed visual aids that the Kadian sales representatives use during the visits, and Actavis noted that doctors associate Kadian with less

abuse and no highs, in comparison to other opioids. Numerous marketing surveys of doctors in 2010 and 2012, for example, confirmed Actavis's messaging about Kadian's purported low addiction potential, and that it had less abuse potential than other similar opioids.

434. A guide for prescribers under Actavis's copyright deceptively represents that Kadian is more difficult to abuse and less addictive than other opioids. The guide includes the following statements: 1) "unique pharmaceutical formulation of KADIAN may offer some protection from extraction of morphine sulfate for intravenous use by illicit users," and 2) KADIAN may be less likely to be abused by health care providers and illicit users" because of "Slow onset of action," "Lower peak plasma morphine levels than equivalent doses of other formulations of morphine," "Long duration of action," and "Minimal fluctuations in peak to trough plasma levels of morphine at steady state." These statements convey both that (1) Kadian does not cause euphoria and therefore is less addictive and that (2) Kadian is less prone to tampering and abuse, even though Kadian was not approved by the FDA as abuse deterrent, and, upon information and belief, Actavis had no studies to suggest it was.

vi. Mallinckrodt's misrepresentations regarding addiction risk

435. As described below, Mallinckrodt promoted its branded opioids Exalgo and Xartemis XR, and opioids generally, in a campaign that consistently mischaracterized the risk of addiction. Mallinckrodt did so through its website and sales force, as well as through unbranded communications distributed through the "C.A.R.E.S. Alliance" it created and led.

436. Mallinckrodt in 2010 created the C.A.R.E.S. (Collaborating and Acting Responsibly to Ensure Safety) Alliance, which it describes as "a coalition of national patient safety, provider and drug diversion organizations that are focused on reducing opioid pain medication abuse and increasing responsible prescribing habits." The "C.A.R.E.S. Alliance" itself is a service mark of Mallinckrodt LLC (and was previously a service mark of Mallinckrodt, Inc.)

copyrighted and registered as a trademark by Covidien, its former parent company. Materials distributed by the C.A.R.E.S. Alliance, however, include unbranded publications that do not disclose a link to Mallinckrodt.

437. By 2012, Mallinckrodt, through the C.A.R.E.S. Alliance, was promoting a book titled *Defeat Chronic Pain Now!* This book is still available online. The false claims and misrepresentations in this book include the following statements:

- "Only rarely does opioid medication cause a true addiction when prescribed appropriately to a chronic pain patient who does not have a prior history of addiction."
- "It is currently recommended that every chronic pain patient suffering from moderate to severe pain be viewed as a potential candidate for opioid therapy."
- "When chronic pain patients take opioids to treat their pain, they rarely develop a true addiction and drug craving."
- "Only a minority of chronic pain patients who are taking long-term opioids develop tolerance."
- "**The bottom line:** Only rarely does opioid medication cause a true addiction when prescribed appropriately to a chronic pain patient who does not have a prior history of addiction."
- "Here are the facts. It is very uncommon for a person with chronic pain to become 'addicted' to narcotics IF (1) he doesn't have a prior history of any addiction and (2) he only takes the medication to treat pain."
- "Studies have shown that many chronic pain patients can experience significant pain relief with tolerable side effects from opioid narcotic medication when taken daily and no addiction."

438. In a 2013 *Mallinckrodt Pharmaceuticals Policy Statement Regarding the Treatment of Pain and Control of Opioid Abuse*, which is still available online, Mallinckrodt stated that, "[s]adly, even today, pain frequently remains undiagnosed and either untreated or undertreated" and cites to a report that concludes that "the majority of people with pain use their

prescription drugs properly, are not a source of misuse, and should not be stigmatized or denied access because of the misdeeds or carelessness of others."

439. Marketing Defendants' suggestions that the opioid epidemic is the result of bad patients who manipulate doctors to obtain opioids illicitly helped further their marketing scheme, but is at odds with the facts. While there are certainly patients who unlawfully obtain opioids, they are a small minority. For example, patients who "doctor-shop"—i.e., visit multiple prescribers to obtain opioid prescriptions—are responsible for roughly 2% of opioid prescriptions. The epidemic of opioid addiction and abuse is overwhelmingly a problem of false marketing (and unconstrained distribution) of the drugs, not problem patients.

440. Marketing Defendants' efforts to trivialize the risk of addiction were, and remain, unsupported by scientific evidence. Studies have shown that at least 8-12%, and as many as 30-40% of long-term users of opioids experience problems with addiction. According to one study, nearly 60% of patients who used opioids for 90 days continued to use opioids five years later.[110] Addiction can result from the use of any opioid, "even at recommended dose"[111] and the risk increases with chronic (more than three months) use. The CDC has emphasized that "continuing opioid therapy for 3 months substantially increases risk for opioid use disorder."[112]

Falsehood #2: Signs of addiction are "pseudoaddiction," requiring more opioids

441. Marketing Defendants covered up the occurrence of addiction by attributing it to a made-up condition they called "pseudoaddiction." Signs of addiction, including shopping for doctors willing to newly write or refill prescriptions for opioids or seeking early refills, actually

reflected undertreated pain that should be addressed with more opioids—the medical equivalent of fighting fire by adding fuel.

442. Purdue, through its unbranded imprint *Partners Against Pain*,[113] promoted the concept of pseudoaddiction through at least 2013 on its website. It disseminated the Definitions Related to the Use of Opioids for the Treatment of Pain section of an American Pain Society ("APS") consensus statement through the website, where APS, who received funding from Defendants, defined pseudoaddiction in the same terms endorsed by Purdue:

> Physical dependence, tolerance, and addiction are discrete and different phenomena that are often confused . . . Pseudoaddiction is a term which has been used to describe patient behaviors that may occur when pain is undertreated. Patients with unrelieved pain may become focused on obtaining medications, may 'clock watch,' and may otherwise seem inappropriately 'drug seeking.' Even such behaviors as illicit drug use and deception can occur in the patient's efforts to obtain relief. Pseudoaddiction can be distinguished from true addiction in that the behaviors resolve when pain is effectively treated. . . . A patient who is physically dependent on opioids may sometimes continue to use these [medications] despite resolution of pain only to avoid withdrawal. Such use does not necessarily reflect addiction.

443. The Federation of State Medical Boards ("FSMB"), a trade organization representing state medical boards, finances opioid- and pain-specific programs through grants from Defendants. A 2004 version of the FSMB *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain* ("FSMB Guidelines"), and the 2007 book adapted from them, *Responsible Opioid Prescribing*, advanced the concept of pseudoaddiction.

[113] *Partners Against Pain* consists of both a website, styled as an "advocacy community" for better pain care, and medical education resources distributed to prescribers by the sales force. It has existed since at least the early 2000s and has been a vehicle for Purdue to downplay the risks of addiction from long-term opioid use. One early pamphlet, for example, answered concerns about OxyContin's addictiveness by claiming: "Drug addiction means using a drug to get 'high' rather than to relieve pain. You are taking opioid pain medication for medical purposes. The medical purposes are clear and the effects are beneficial, not harmful."

444. *Responsible Opioid Prescribing* was sponsored by Purdue, Endo, and Teva. The FSMB website described the book as the "leading continuing medical education (CME) activity for prescribers of opioid medications." In all, more than 163,000 copies of *Responsible Opioid Prescribing* were distributed nationally.

445. Janssen sponsored, funded, and edited the *Let's Talk Pain* website, which in 2009 stated: "pseudoaddiction . . . refers to patient behaviors that may occur when *pain is under-treated* . . . . Pseudoaddiction is different from true addiction because such behaviors can be resolved with effective pain management." This website was accessible online until May 2012.

446. Endo sponsored a National Initiative on Pain Control (NIPC) CME program in 2009 titled *Chronic Opioid Therapy: Understanding Risk While Maximizing Analgesia*, which promoted pseudoaddiction by teaching that a patient's aberrant behavior was the result of untreated pain. Endo substantially controlled NIPC, an initiative run by the APF, by funding NIPC projects; developing, specifying, and reviewing its content; and distributing NIPC materials. APF internal documents show that APF viewed the NIPC as an "opportunity to generate new revenue" given Endo's funding commitment.

447. Marketing Defendants also promoted the concept of pseudoaddiction through Dr. Russell Portenoy, a leading KOL for the Defendants. In doing so, he popularized the concept and falsely claimed that pseudoaddiction is substantiated by scientific evidence.

448. The FAQs section of *pain-topics.org*, a now-defunct website to which Mallinckrodt provided funding, also contained misleading information about pseudoaddiction. Specifically, the website advised providers to "keep in mind" that signs of potential drug diversion, rather than signaling "actual" addiction, "may represent pseudoaddiction," which the website described as

behavior that occurs in patients when pain is "undertreated" and includes patients becoming "very focused on obtaining opioid medications and may be erroneously perceived as 'drug seeking.'"

449. The CDC Guideline for prescribing opioids for chronic pain, a "systematic review of the best available evidence" by a panel excluding experts with conflicts of interest, rejects the concept of pseudoaddiction. The Guideline nowhere recommends that opioid doses be increased if a patient is not experiencing pain relief. To the contrary, the Guideline explains that "[p]atients who do not experience clinically meaningful pain relief early in treatment . . . are unlikely to experience pain relief with longer-term use,"[114] and that physicians should "reassess[] pain and function within 1 month" in order to decide whether to "minimize risks of long-term opioid use by discontinuing opioids" because the patient is "not receiving a clear benefit."[115]

Falsehood #3: To the extent there is a risk of addiction, it can be easily identified and managed

450. Marketing Defendants falsely instructed prescribers and patients that screening tools, patient contracts, urine drug screens, and similar strategies allow health care providers to safely prescribe opioids to patients, including patients predisposed to addiction, and failed to disclose the lack of evidence that these strategies actually work to mitigate addiction risk. By using screening tools, these Defendants advised doctors that they could identify patients likely to become addicted and safely prescribe to everyone else.

451. Such misrepresentations regarding safe opioid prescribing made health care providers more comfortable prescribing opioids to their patients and patients more comfortable starting chronic opioid therapy. These misrepresentations were especially insidious because Defendants aimed them at general practitioners and family doctors who lack the time and expertise

[114] CDC Guideline at 13.
[115] *Id.* at 25.

to closely manage higher-risk patients on opioids. Moreover, these misrepresentations allowed doctors to believe opioid addiction was the result of other prescribers failing to rigorously manage and weed out problem patients, not a risk inherent to the drugs.

452. These Defendants conveyed these safe prescribing messages in nationally distributed marketing materials. A catalogue distributed by Purdue to prescribers across the country and, on information and belief, in the City, included information on screening tools. On information and belief, none of the Defendants disclosed the lack of evidence for efficacy of these tools.

453. Marketing Defendants also promoted screening tools as a reliable means to manage addiction risk in CME programs and scientific conferences, which would have been attended by or were available online, to Huntington prescribers.

454. For example, Purdue sponsored a 2011 CME program titled Managing Patient's Opioid Use: Balancing the Need and Risk. This presentation deceptively instructed prescribers that screening tools, patient agreements, and urine tests prevented "overuse of prescriptions" and "overdose deaths." Purdue also funded a 2012 CME program called Chronic Pain Management and Opioid Use: Easing Fears, Managing Risks, and Improving Outcomes. The presentation deceptively instructed doctors that, through the use of screening tools, more frequent refills, and other techniques, even high-risk patients showing signs of addiction could be treated with opioids.

455. Purdue used its involvement in the College on the Problems of Drug Dependence ("CPDD"), which promotes scientific research and professional development to support addiction prevention professionals, to promote the idea that addiction risk can be managed. A Purdue employee served on the CPDD board of directors. Purdue presented a disproportionate number of talks—with very different messages from non-Purdue talks—at CPDD conferences. One of

Purdue's consistent themes is that "bad apple" patients, not opioids, are the source of the opioid crisis, and that once those patients are identified doctors can safely prescribe opioids without a risk of addiction. Hundreds of addiction treatment specialists from across the country and, upon information and belief, from the City, attended these conferences.

456. Endo paid for a 2007 supplement in the Journal of Family Practice written by a doctor who became a member of Endo's speakers' bureau (doctors paid to give talks, typically reserved for the largest prescribers) in 2010. The supplement, entitled *Pain Management Dilemmas in Primary Care: Use of Opioids*, emphasized the effectiveness of screening tools, claiming that patients at high risk of addiction could safely receive chronic opioid therapy using a "maximally structured approach" involving toxicology screens and pill counts.

457. The CDC Guideline confirmed the falsity of Marketing Defendants' claims about the utility of patient screening and management strategies in managing addiction risk. The Guideline notes that there are no studies assessing the effectiveness of risk mitigation strategies—such as screening tools or patient contracts—"for improving outcomes related to overdose, addiction, abuse, or misuse." The CDC Guideline recognized that available risk screening tools "show insufficient accuracy for classification of patients as at low or high risk for [opioid] abuse or misuse" and counseled that doctors "should not overestimate the ability of these tools to rule out risks from long-term opioid therapy."[116]

Falsehood #4: Opioid withdrawal can be avoided by tapering

458. Purdue's profits, and, upon information and belief, the profits of the other Marketing Defendants, depend on keeping patients on opioids on an ongoing basis. According to internal documents, 87% of Purdue's OxyContin business is driven by continuing prescriptions.

[116] CDC Guideline at 28 (emphasis added).

Thus, recurring prescriptions to chronic pain patients is a key component of Purdue's business model.

459. To convince prescribers and patients that opioids should be used to treat chronic pain, Defendants had to persuade them of a significant upside to long-term opioid use. Assessing existing evidence, the CDC Guideline found that there is "insufficient evidence to determine the long-term benefits of opioid therapy for chronic pain."[117] In fact, the CDC found that "[n]o evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later (with most placebo-controlled randomized trials ≤ 6 weeks in duration)"[118] and that other treatments were more or equally beneficial and less harmful than long-term opioid use. The FDA, too, has recognized the lack of evidence to support long-term opioid use. In 2013, the FDA stated that it was "not aware of adequate and well-controlled studies of opioids use longer than 12 weeks."[119] As a result, the CDC recommends that opioids not be used in the first instance and for treatment of chronic pain; rather, opioids should be used only after prescribers have exhausted alternative treatments.

460. Nevertheless, upon information and belief, Marketing Defendants touted the purported benefits of long-term opioid use, while falsely and misleadingly suggesting that these benefits were supported by scientific evidence.

461. In addition, two prominent professional medical membership organizations, the American Pain Society ("APS") and the American Academy of Pain Medicine ("AAPM"), each received substantial funding from Marketing Defendants. According to a letter from U.S. Senate Committee on Finance Ranking Member Ron Wyden to Secretary Thomas Price of the U.S.

[117] *Id.* at 10.
[118] *Id.* at 9.
[119] Woodcock Letter, *supra*.

Department of Health & Human Services, as recently as May 2017, the Corporate Council of AAPM included Endo, Janssen, Purdue and Teva, along with several other pharmaceutical drug companies.[120] Upon information and belief, Marketing Defendants exercised considerable influence over their work on opioids. Both organizations issued a consensus statement in 1997, *The Use of Opioids for the Treatment of Chronic Pain*, which endorsed opioids to treat chronic pain and claimed that the risk that patients would become addicted to opioids was low. The co-author of the statement, Dr. David Haddox, was at the time a paid speaker for Purdue and later became a senior executive for the company. KOL Dr. Portenoy was the sole consultant. The consensus statement remained on AAPM's website until 2011 and was only removed from AAPM's website after a doctor complained.

462. A past president of the AAPM, Dr. Scott Fishman, who also served as a KOL for Marketing Defendants, stated that he would place the organization "at the forefront" of teaching that "the risks of addiction are . . . small and can be managed."[121]

463. AAPM and APS issued treatment guidelines in 2009 ("AAPM/APS Guidelines") which continued to recommend the use of opioids to treat chronic pain. Treatment guidelines, like the AAPM/APS Guidelines, were particularly important to Marketing Defendants in securing acceptance for chronic opioid therapy. They are relied upon by doctors, especially general practitioners and family doctors who have no specific training in treating chronic pain. Six of the twenty-one panel members who drafted the AAPM/APS Guidelines received support from Purdue, eight from Teva, nine from Janssen, and ten from Endo.

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[120] Letter from Ron Wyden, Ranking Member, U.S. Senate Committee on Finance, to Honorable Thomas E. Price, Secretary, U.S. Health & Human Services (May 5, 2017), https://www.finance.senate.gov/imo/media/doc/050817%20corrected%20Senator%20Wyden%20to%20Secretary%20Price%20re%20FDA%20Opioid%20Prescriber%20Working%20Group%20(5%20May%202017).pdf.

[121] Interview by Paula Moyer with Scott M. Fishman, M.D., Professor of Anesthesiology and Pain Medicine, Chief of the Division of Pain Medicine, Univ. of Cal., Davis (2005), available at http://www.medscape.org/viewarticle/500829.

464. The AAPM/APS Guidelines promote opioids as "safe and effective" for treating chronic pain. The panel made "strong recommendations" despite "low quality of evidence" and concluded that the risk of addiction is manageable for patients, even with a prior history of drug abuse. One panel member, Dr. Joel Saper, Clinical Professor of Neurology at Michigan State University and founder of the Michigan Headache & Neurological Institute, resigned from the panel because of his concerns that the Guidelines were influenced by contributions that drug companies, including Purdue, Endo, Janssen, and Teva, made to the sponsoring organizations and committee members.

465. Dr. Gilbert Fanciullo, now retired as a professor at Dartmouth College's Geisel School of Medicine, who served on the AAPM/APS Guidelines panel, has since described them as "skewed" by drug companies and "biased in many important respects," including the high presumptive maximum dose, lack of suggested mandatory urine toxicology testing, and claims of a low risk of addiction.

466. The AAPM/APS Guidelines are still available online, were reprinted in the *Journal of Pain*, and have influenced not only treating physicians, but also the body of scientific evidence on opioids. According to Google Scholar, they have now been cited at least 1,647 times in academic literature. These Guidelines were available to Huntington prescribers.

467. Purdue specifically marketed its opioids for chronic pain conditions such as low back pain and osteoarthritis, using "vignettes," or patient exemplars, illustrating the use of opioids to treat patients with these conditions, and inviting doctors to identify patients with these conditions as appropriate candidates for its opioids. Purdue also acknowledged its strategy to encourage prescribers to switch patients from nonsteroidal anti-inflammatory drugs ("NSAIDs,"

over-the-counter, non-narcotic pain relievers such as ibuprofen) through articles in "reputable journals" such as AAPM's and "hearing from respected physicians."

468. Purdue also published misleading studies to enhance the perception that opioids are effective long-term for chronic pain conditions. One study asserts that OxyContin is safe and effective for the chronic pain condition osteoarthritis. The study, sponsored by Purdue, involved providing oxycodone for 30 days, and then randomizing participants and providing a placebo, an immediate release oxycodone with acetaminophen (like Percocet), or OxyContin. Only 107 of the 167 patients went on to the second phase of the study, and most who withdrew left because of adverse events (nausea, vomiting, drowsiness, dizziness, or headache) or ineffective treatment. Despite relating to a chronic condition, opioids were provided only short-term. The authors even acknowledge that the "results . . . should be confirmed in trials of longer duration to confirm the role of opioids in a chronic condition such as OA [osteoarthritis]."[122] Yet, the authors conclude that "[t]his clinical experience shows that opioids were well tolerated with only rare incidence of addiction and that tolerance to the analgesic effects was not a clinically significant problem when managing patients with opioids long-term."[123] This statement is not supported by the data—a substantial proportion of patients dropped out because of adverse effects, there was no reported data regarding addiction, and the study was not long-term.

469. Teva deceptively marketed its opioids Actiq and Fentora for chronic pain even though the FDA has expressly limited their use to the treatment of cancer pain in opioid-tolerant individuals.

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[122] Jacques R. Caldwell, *et al.*, *Treatment of Osteoarthritis Pain with Controlled Release Oxycodone or Fixed Combination Oxycodone Plus Acetaminophen Added to Nonsteroidal Antiinflammatory Drugs: A Double Blind, Randomized, Multicenter, Placebo Controlled Trial*, 266.4 Journal of Rheumatology 862-869 (1999).
[123] *Id.*

470. Both Actiq and Fentora are extremely powerful fentanyl-based opioids. Neither is approved for or has been shown to be safe or effective for chronic pain. Indeed, the FDA expressly prohibited Teva from marketing Actiq for anything but cancer pain, and refused to approve Fentora for the treatment of chronic pain because of the potential harm, including the high risks of "serious and life-threatening adverse events" and abuse—which are greatest in non-cancer patients. The FDA also issued a Public Health Advisory in 2007 emphasizing that Fentora should only be used for cancer patients who are opioid-tolerant and should not be used for any other conditions, such as migraines, post-operative pain, or pain due to injury.

471. Despite this, Teva has conducted a well-funded and deceptive campaign to promote Actiq and Fentora for chronic pain and other non-cancer conditions for which it was not approved, appropriate, or safe. This campaign included the use of CMEs, speaker programs, KOLs, and journal supplements to give doctors the false impression that Actiq and Fentora are safe and effective for treating non-cancer pain, without disclosing the lack of evidence or the FDA's rejection of their use for chronic pain.

472. For example, Teva paid to have a CME it sponsored, *Opioid-Based Management of Persistent and Breakthrough Pain*, published in a supplement of Pain Medicine News in 2009. The CME instructed doctors that "clinically, broad classification of pain syndromes as either cancer- or noncancer-related has limited utility" and recommended Actiq and Fentora for patients with chronic pain. The CME is still available online.

473. Teva's sales representatives set up hundreds of speaker programs for doctors, including many non-oncologists, which promoted Actiq and Fentora for the treatment of non-cancer pain.

474. In December 2011, Teva widely disseminated a journal supplement entitled *"Special Report: An Integrated Risk Evaluation and Mitigation Strategy for Fentanyl Buccal Tablet (FENTORA) and Oral Transmucosal Fentanyl Citrate (ACTIQ)"* to Anesthesiology News, Clinical Oncology News, and Pain Medicine News—three publications that are sent to thousands of anesthesiologists and other medical professionals nationally, including, upon information and belief, in the City. The Special Report openly promotes Fentora for "multiple causes of pain," and not just cancer pain.

475. Teva's deceptive marketing gave doctors and patients the false impression that Actiq and Fentora were not only safe and effective for treating chronic pain, but also were approved by the FDA for such uses.

476. On December 28, 2011, the FDA mandated a Risk Evaluation and Mitigation Strategy (REMS) for the class of products for which Teva's Actiq and Fentora belong, Transmucosal Immediate Release Fentanyl (TIRF). The TIRF REMS programs include mandatory patient and prescriber enrollment forms, as well as certification requirements for prescribers. The forms are not comprehensive and do not, for instance, disclose that addiction can develop when the medications are used as prescribed, nor do they disclose that risks are greatest at higher doses—and patients must already be taking high doses of opioids to be prescribed Actiq and Fentora.

Falsehood #5: Long-term opioid use improves functioning

477. Marketing Defendants also claimed—without evidence—that long-term opioid use would help patients resume their lives and jobs.

478. Marketing Defendants' materials that, upon information and belief, were distributed or made available in the City, reinforced this message. The 2011 publication *A Policymaker's Guide* falsely claimed that "multiple clinical studies have shown that opioids are

effective in improving" "[d]aily function" and "[o]verall health-related quality of life for people with chronic pain." A series of medical journal advertisements for OxyContin in 2012 presented "Pain Vignettes"—case studies featuring patients with pain conditions persisting over several months—that implied functional improvement. For example, one advertisement described a "writer with osteoarthritis of the hands" and implied that OxyContin would help him work more effectively. Similarly, starting in at least May of 2011, Endo distributed and made available on its website, opana.com, a pamphlet promoting Opana ER with photographs depicting patients with physically demanding jobs like construction worker and chef, misleadingly implying that the drug would provide long-term pain-relief and functional improvement.

479. Additional illustrative examples are described below:

a. Janssen sponsored and edited a patient education guide entitled Finding Relief: Pain Management for Older Adults (2009), which states as "a fact" that "opioids may make it easier for people to live normally." The guide lists expected functional improvements from opioid use, including sleeping through the night, returning to work, recreation, sex, walking, and climbing stairs and states that "[u]sed properly, opioid medications can make it possible for people with chronic pain to 'return to normal.'"

b. Responsible Opioid Prescribing (2007), sponsored and distributed by Teva, Endo and Purdue, taught that relief of pain by opioids, by itself, improved patients' function. The book remains for sale online.

c. Purdue and Teva sponsored APF's Treatment Options: A Guide for People Living with Pain (2007), which counseled patients that opioids "give [pain patients] a quality of life we deserve." The guide was available online until APF shut its doors in May 2012.

d. Endo's NIPC website painknowledge.com claimed in 2009 that with opioids, "your level of function should improve; you may find you are now able to participate in activities of daily living, such as work and hobbies, that you were not able to enjoy when your pain was worse." Elsewhere, the website touted improved quality of life (as well as "improved function") as benefits of opioid therapy. The grant request that Endo approved for this project specifically indicated NIPC's intent to make claims of functional improvement, and Endo closely tracked visits to the site.

e. Endo was the sole sponsor, through NIPC, of a series of CMEs titled Persistent Pain in the Older Patient, which claimed that chronic opioid therapy has been "shown to reduce pain and improve depressive symptoms and cognitive functioning." The CME was disseminated via webcast.

480. Mallinckrodt followed suit, stating on its website, in a section on "responsible use" of opioids, claims that "[t]he effective pain management offered by our medicines helps enable patients to stay in the workplace, enjoy interactions with family and friends, and remain an active member of society."124

481. Likewise, Marketing Defendants' claims that long-term use of opioids improves patient function and quality of life are unsupported by clinical evidence. As noted above, there are no controlled studies of the use of opioids beyond 16 weeks, and there is no evidence that opioids improve patients' pain and function long-term. On the contrary, the available evidence indicates opioids are not effective to treat chronic pain, and may worsen patients' health and pain. Increasing the duration of opioid use is strongly associated with an increasing prevalence of mental health conditions (depression, anxiety, post-traumatic stress disorder, and substance abuse), increased psychological distress, and greater health care utilization.

482. As one pain specialist observed, "opioids may work acceptably well for a while, but over the long term, function generally declines, as does general health, mental health, and social functioning. Over time, even high doses of potent opioids often fail to control pain, and these patients are unable to function normally."125 Studies of patients with lower back pain and migraine headaches, for example, have consistently shown that patients experienced deteriorating

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124 Mallinckrodt Pharmaceuticals, Responsible Use, http://www.mallinckrodt.com/corporate-responsibility/responsible-use

125 Andrea Rubinstein, *Are We Making Pain Patients Worse?*, Sonoma Med. (Fall 2009), available at http://www.nbcms.org/about-us/sonoma-county-medical-association/magazine/sonoma-medicine-are-we-making-pain-patients-worse*?*.

function over time, as measured by ability to return to work, physical activity, pain relief, rates of depression, and subjective quality-of-life measures. Analyses of workers' compensation claims have found that workers who take opioids are almost four times more likely to reach costs over $100,000, stemming from greater side effects and slower returns to work. According to these studies, receiving an opioid for more than seven days also increased patients' risk of being on work disability one year later.

483. The FDA and other federal agencies have, for years, made clear the lack of evidence for claims that the use of opioids for chronic pain improves patients' function and quality of life.126 The CDC Guideline, following a "systematic review of the best available evidence," concluded that "[w]hile benefits for pain relief, function and quality of life with long-term opioid use for chronic pain are uncertain, risks associated with long-term opioid use are clearer and significant."127 According to the CDC, "for the vast majority of patients, the known, serious, and too-often-fatal risks far outweigh the unproven and transient benefits [of opioids for chronic pain]."[128]

Falsehood #6: Alternative forms of pain relief pose greater risks than opioids

484. In materials Defendants produced, sponsored, or controlled, these Defendants omitted known risks of chronic opioid therapy and emphasized or exaggerated risks of competing

[126] The FDA has warned other drug makers that claims of improved function and quality of life were misleading. *See* Warning Letter from Thomas Abrams, Dir., FDA Div. of Mktg., Adver., & Commc'ns, to Doug Boothe, CEO, Actavis Elizabeth LLC (Feb. 18, 2010), (rejecting claims that opioid manufacturer Actavis' opioid, Kadian, had an "overall positive impact on a patient's work, physical and mental functioning, daily activities, or enjoyment of life."); Warning Letter from Thomas Abrams, Dir., FDA Div. of Mktg., Adver., & Commc'ns, to Brian A. Markison, Chairman, President and Chief Executive Officer, King Pharmaceuticals, Inc. (March 24, 2008), (finding the claim that "patients who are treated with [Avinza (morphine sulfate ER)] experience an improvement in their overall function, social function, and ability to perform daily activities . . . has not been demonstrated by substantial evidence or substantial clinical experience."). The FDA's warning letters were available to Defendants on the FDA website.

[127] CDC Guideline at 2, 18.

[128] Thomas R. Frieden and Debra Houry, *Reducing the Risks of Relief—The CDC Opioid-Prescribing Guideline*, NEJM, Apr. 21, 2016 at 1503.

products so that prescribers and patients would be more likely to choose opioids and would favor opioids over other therapies such as over-the-counter acetaminophen or NSAIDs. None of these claims were corroborated by scientific evidence. In fact, several studies have shown that ibuprofen and acetaminophen taken together are better than opioids at relieving pain such as dental pain, low back pain, and moderate acute traumatic pain.[129]

485. In addition to failing to disclose in promotional materials the risks of addiction, abuse, overdose, and death, Marketing Defendants routinely ignored other risks, such as hyperalgesia, a "known serious risk associated with chronic opioid analgesic therapy,"[130] in which the patient becomes more sensitive to pain over time; hormonal dysfunction; decline in immune function; mental clouding, confusion, and dizziness; increased falls and fractures in the elderly; neonatal abstinence syndrome (when an infant exposed to opioids prenatally withdraws from the drugs after birth); and potentially fatal interactions with alcohol or benzodiazepines, which are used to treat post-traumatic stress disorder and anxiety (conditions that often accompany chronic pain symptoms).

486. Purdue and Teva sponsored APF's *Treatment Options: A Guide for People Living with Pain* (2007), which counseled patients that opioids differ from NSAIDs in that they have "no ceiling dose" and are therefore the most appropriate treatment for severe pain. The publication inaccurately attributes 10,000 to 20,000 deaths annually to NSAIDs (the actual figure is approximately 3,200—far fewer than from opioids).[131] This publication also warned that risks of NSAIDs increase if "taken for more than a period of months," with no corresponding warning about opioids.

[129] Donald Teater, M.D., *Evidence for the Efficacy of Pain Medication*, National Safety Council, October 2014.
[130] *See* Martin, *supra*.
[131] The higher figure reflects deaths from all causes.

487. APF's *Exit Wounds*, sponsored by Purdue and Endo and aimed at veterans, omits warnings of the potentially fatal risk of interactions between opioids and benzodiazepines, a class of drug commonly prescribed to veterans with post-traumatic stress disorder. This book is available from Amazon.com and other retailers.

488. Purdue and Endo sponsored a CME program, *Overview of Management Options*, published by the American Medical Association in 2003, 2007, 2010, and 2013, and discussed further below. The CME was edited by Dr. Russell Portenoy, among others, and taught that NSAIDs and other drugs, but not opioids, are unsafe at high doses.

489. Marketing Defendants frequently contrasted the lack of a ceiling dosage for opioids with the risks of NSAIDs. These Defendants deceptively describe the risks from NSAIDs while failing to disclose the risks from opioids. (*See e.g.*, *Case Challenges in Pain Management: Opioid Therapy for Chronic Pain* (Endo) [describing massive gastrointestinal bleeds from long-term use of NSAIDs and recommending opioids]; *Finding Relief: Pain Management for Older Adults* (Janssen) [NSAIDs caused kidney or liver damage and increased risk of heart attack and stroke, versus opioids, which cause temporary "upset stomach or sleepiness" and constipation].)

490. These omissions are significant and material to patients and prescribers. A Cochrane Collaboration review of evidence relating to the use of opioids for chronic pain found that 22.9% of patients in opioid trials dropped out before the study began because of the "adverse effects" of opioids.[132]

491. Again, Marketing Defendants' misrepresentations were effective. A study of 7.8 million doctor visits nationwide between 2000 and 2010 found that opioid prescriptions increased

[132] Meredith Noble M., *Long-Term Opioid Management for Chronic Noncancer Pain (Review)*, Cochrane Database of Systematic Reviews, Issue 1, 11 (2010).

from 11.3% to 19.6% of visits while NSAID and acetaminophen prescriptions fell from 38% to 29%. The CDC reports that the quantity of opioids dispensed per capita tripled from 1999 to 2015.

Falsehood #7: Opioid doses can be increased without limit or greater risks

492. Marketing Defendants falsely claimed to prescribers and consumers that opioids could be taken in ever-increasing strengths to obtain pain relief, without disclosing that higher doses increased the risk of addiction and overdose. This was particularly important because patients on opioids for more than a brief period develop tolerance, requiring increasingly high doses to achieve pain relief. These Defendants needed to generate a comfort level among doctors to ensure the doctors maintained patients on the drugs even at the high doses that became necessary. Further, as described in more detail below, Purdue encouraged doctors to prescribe higher doses, rather than prescribe OxyContin more frequently than twice-a-day—despite knowing that OxyContin frequently did not provide 12 hours of relief.

493. Purdue-sponsored publications and CMEs available online also misleadingly suggested that higher opioid doses carried no added risk.

494. Through at least June 2015, Purdue's *In the Face of Pain* website promoted the notion that if a patient's doctor did not prescribe a sufficient dose of opioids, the patient should see different doctors until finding a doctor who would.

495. *A Policymaker's Guide,* the 2011 publication on which, upon information and belief, Purdue collaborated with APF, taught that dose escalations are "sometimes necessary," but it did not disclose the risks from high dose opioids. Until recently, this publication was still available online.[133]

[133] *See* http://s3.documentcloud.org/documents/277603/apf-policymakers-guide.pdf (last visited Aug. 17, 2018).

496. The Purdue-sponsored CME, *Overview of Management Options*, discussed above, again instructed physicians that NSAIDs (like ibuprofen) are unsafe at high doses (because of risks to patients' kidneys), but it did not disclose risks from opioids at high doses.

497. Endo sponsored a website, painknowledge.com, which claimed in 2009 that opioid dosages may be increased until "you are on the right dose of medication for your pain."

498. Endo distributed a pamphlet edited by Dr. Russell Portenoy entitled *Understanding Your Pain: Taking Oral Opioid Analgesics*, which appeared on Endo's website. In Q&A format, it asked "If I take the opioid now, will it work later when I really need it?" The response is, "The dose can be increased. . . . You won't 'run out' of pain relief."

499. Janssen sponsored a patient education guide entitled *Finding Relief: Pain Management for Older Adults* (2009), which was distributed by its sales force. This guide listed dosage limitations as "disadvantages" of other pain medicines but omitted any discussion of risks of increased opioid dosages.

500. These claims conflict with the scientific evidence. Patients receiving high doses of opioids (*e.g.*, doses greater than 100 mg morphine equivalent dose ("MED") per day) as part of long-term opioid therapy are three to nine times more likely to suffer overdose from opioid-related causes than those on low doses. As compared to available alternative pain remedies, scholars have suggested that tolerance to the respiratory depressive effects of opioids develops at a slower rate than tolerance to opioids' analgesic effects. Accordingly, the practice of continuously escalating doses to match pain tolerance can, in fact, lead to overdose even where opioids are taken as recommended.

501. The CDC Guideline concludes that the "[b]enefits of high-dose opioids for chronic pain are not established" while "there is an increased risk for serious harms related to long-term

opioid therapy that appears to be dose-dependent."[134] That is why the CDC advises doctors to "avoid increasing doses" above 90 mg MED.[135]

Falsehood #8: OxyContin provides twelve hours of pain relief

502. To convince prescribers and patients to use OxyContin, Purdue misleadingly promoted the drug as providing 12 continuous hours of pain relief with each dose. In reality, OxyContin does not last for 12 hours in many patients, a fact Purdue has known since the product's launch.

503. OxyContin has been FDA-approved for twice-daily—"Q12"—dosing frequency since its debut in 1996. Purdue sought that dosing frequency in order to maintain a competitive advantage over more frequently dosed opioids. Even so, Purdue has gone well beyond the label's instructions to take OxyContin every 12 hours. Purdue has affirmatively claimed in its general marketing, including, upon information and belief, to prescribers in the City, that OxyContin lasts for 12 hours and that this is a key advantage of OxyContin, implying that most or all patients would in fact experience continuous pain relief for the full 12 hour dose period. Purdue has also failed to disclose that OxyContin fails to provide 12 hours of pain relief to many patients. These misrepresentations, which Purdue continues to make, are particularly dangerous because inadequate dosing helps fuel addiction, as explained below.

504. From the outset, Purdue leveraged 12-hour dosing to promote OxyContin as providing continuous, round-the-clock pain relief with the convenience of not having to wake to take a third or fourth pill. The 1996 press release for OxyContin touted 12-hour dosing as

[134] CDC Guideline at 19. The 2016 CDC Guideline reinforces earlier findings announced by the FDA. In 2013, the FDA acknowledged "that the available data do suggest a relationship between increasing opioid dose and risk of certain adverse events." For example, the FDA noted that studies "appear to credibly suggest a positive association between high-dose opioid use and the risk of overdose and/or overdose mortality."
[135] CDC Guideline at 16.

providing "smooth and sustained pain control all day and all night." But the FDA has never approved such a marketing claim. To the contrary, the FDA found in 2008, in response to a Citizen Petition by the Connecticut Attorney General, that a "substantial number" of chronic pain patients taking OxyContin experienced "end of dose failure"—*i.e.*, little or no pain relief at the end of the dosing period.

505. Moreover, Purdue itself long has known, dating to its development of OxyContin, that the drug wears off well short of 12 hours in many patients. In one early Purdue clinical trial, a third of patients dropped out because the treatment was ineffective. Researchers changed the rules to allow patients to take supplemental painkillers—"rescue doses"—in between OxyContin doses. In another study, most patients used rescue medication, and 95% resorted to it at least once. In other research conducted by Purdue, the drug wore off in under 6 hours in 25% of patients and in under 10 hours in more than 50%.

506. End-of-dose failure renders OxyContin even more dangerous because patients begin to experience withdrawal symptoms, followed by a euphoric rush with their next dose—a cycle that fuels a craving for OxyContin. For this reason, Dr. Theodore Cicero, a neuropharmacologist at the Washington University School of Medicine in St. Louis, has called OxyContin's 12-hour dosing "the perfect recipe for addiction."[136] Many patients will exacerbate this cycle by taking their next dose ahead of schedule or resorting to a rescue dose of another opioid, increasing the overall amount of opioids they are taking.

507. Purdue has remained committed to 12-hour dosing because it is key to OxyContin's market dominance and comparatively high price; without this advantage, the drug had little to offer over less expensive, short-acting opioids. In a 2004 letter to the FDA, Purdue acknowledged that

[136] Harriet Ryan, *'You Want a Description of Hell?' OxyContin's 12-Hour Problem*, L.A. Times, May 5, 2016, available at http://www.latimes.com/projects/oxycontin-part1/.

it had not pursued approval to allow more frequent dosing in the label (*e.g.*, every 8 hours) because 12-hour dosing was "a significant competitive advantage."

508. While Purdue's commitment to marketing opioids as a 12-hour drug made it more addictive, Purdue falsely promoted OxyContin as providing "steady state" relief and less likely than other opioids to create a cycle of crash and cravings that fueled addiction and abuse.

509. Promotion of 12-hour dosing, without disclosing its limitations, is misleading because it implies that the pain relief supplied by each dose lasts 12 hours. FDA approval of OxyContin for 12-hour dosing does not give Purdue license to misrepresent the duration of pain relief it provides to patients; moreover, Purdue had a responsibility to correct its label to reflect appropriate dosing and to disclose to prescribers what it knew about OxyContin's actual duration, but disregarded that responsibility in its pursuit of a marketing advantage.[137]

510. Purdue was also aware of some physicians' practice of prescribing OxyContin more frequently than 12 hours—a common occurrence. Purdue's promoted solution to this problem was to increase the dose, rather than the frequency, of prescriptions, even though higher dosing carries its own risks. According to a CDC clinical evidence review, higher opioid doses are related to increased risks of motor vehicle injury, opioid use disorder, and overdoses, and the increased risk increases in a dose-dependent manner.[138] With higher doses, patients experience higher highs and lower lows, increasing their craving for their next pill. Nationwide, based on an analysis by the *Los Angeles Times*, more than 52% of patients taking OxyContin longer than three months are on

[137] For example, Kadian, an opioid manufactured by Allergan, was designed to be taken once a day, but the label acknowledges and advises dosing of up to every 12 hours for certain patients.

[138] Mark J. Edlund, *The Role of Opioid Prescription in Incident Opioid Abuse and Dependence Among Individuals with Chronic Non-cancer Pain*, 30 Clin. J. Pain 557–564 (2014); Woodcock Letter, *supra*.

doses greater than 60 milligrams per day—which converts to the 90 MED that the CDC Guideline urges prescribers to "avoid" or "carefully justify."[139]

Falsehood #9: New formulations of certain opioids successfully deter abuse

511. Rather than take the widespread abuse and addiction to opioids as reason to cease their untruthful marketing claims and efforts, Defendants Purdue and Endo seized them as a market opportunity. These companies oversold their abuse-deterrent formulations ("ADF") as a solution to opioid abuse and as a reason that doctors could continue to safely prescribe their opioids. Purdue's and Endo's false and misleading marketing of the benefits of its ADF opioids preserved and expanded their sales and influenced prescribers to discount evidence of opioid addiction and abuse and attribute it to other, less safe opioids—thereby prolonging the opioid epidemic in the City.

Purdue's Deceptive Marketing of Reformulated OxyContin and Hysingla ER.

512. Reformulated ADF OxyContin was approved by the FDA in April 2010. It was not until 2013 that the FDA, in response to a Citizen Petition filed by Purdue, permitted reference to the abuse-deterrent properties in its label. However, the FDA made clear that abuse-deterrent properties do not stop tampering but only make it harder to modify the pills. ADF pills can still be snorted and injected if tampered with, and these pills are still sought after by abusers because of their high likability when snorted. Further, ADF properties do not reduce oral abuse—the most common form of abuse—in any way. When Hysingla ER (extended-release hydrocodone) launched in 2014, the product included similar abuse-deterrent properties and limitations.

[139] CDC Guideline at 16.

513. It is unlikely a coincidence that reformulated OxyContin was introduced shortly before generic versions of OxyContin were to become available, threatening to erode Purdue's market share and the price it could charge. Through a Citizen Petition, Purdue was able to secure a determination by the FDA in April 2013 that original OxyContin should be removed from the market as unsafe (lacking abuse-deterrent properties), and thus non-ADF generic copies could not be sold. As a result, Purdue extended its branded exclusivity for OxyContin until the patent protection on the abuse-deterrent coating expires.

514. Purdue nonetheless touted its introduction of ADF opioids as evidence of its good corporate citizenship and commitment to address the opioid crisis. Touting the benefits of ADF opioids, Purdue's website asserts, for instance: "we are acutely aware of the public health risks these powerful medications create . . . That's why we work with health experts, law enforcement, and government agencies on efforts to reduce the risks of opioid abuse and misuse . . . ."[140]

515. Purdue knew or should have known that "reformulated OxyContin is not better at tamper resistance than the original OxyContin"[141] and is still regularly tampered with and abused.

516. Websites and message boards used by drug abusers and others, such as bluelight.org and reddit.com, report a variety of ways to tamper with OxyContin and Hysingla ER, including through grinding, microwaving then freezing, or drinking soda or fruit juice in which a tablet is dissolved. A publicly available Citizen Petition submitted to the FDA in 2016 by a drug manufacturing firm challenged Purdue's abuse-deterrent labeling based on the firm's ability to easily prepare so-called abuse deterrent OxyContin to be snorted or injected.

[140] Purdue website, *Opioids With Abuse-Deterrent Properties*, available at http://www.purduepharma.com/healthcare-professionals/responsible-use-of-opioids/opioids-with-abuse-deterrentproperties/.
[141] Hr'g Test. of Dr. Mohan Rao at 1615:7-10, In re OxyContin, No. 1:04-md-01603-SHS (SDNY Oct. 7, 2013), ECF No. 613.

517. *One-third* of the patients in a 2015 study defeated the ADF mechanism and were able to continue inhaling or injecting the drug. To the extent that the abuse of Purdue's ADF opioids was reduced, there was no meaningful reduction in drug abuse, as many addicts simply shifted to other drugs such as heroin.

518. A 2013 article presented by Purdue employees based on review of data from poison control centers, concluded that ADF OxyContin can reduce abuse, but it ignored important negative findings. The study revealed that abuse merely shifted to other drugs and that, when the actual incidence of harmful exposures was calculated, there were *more* harmful exposures to opioids (including heroin) after the reformulation of OxyContin. In short, the article deceptively emphasized the advantages and ignored the disadvantages of ADF OxyContin.

519. The CDC Guideline confirms that "*[n]o* studies" support the notion that "abuse-deterrent technologies [are] a risk mitigation strategy for deterring or preventing abuse," noting that the technologies "do not prevent opioid abuse through oral intake, the most common route of opioid abuse, and can still be abused by non-oral routes."[142] Tom Frieden, the Director of the CDC, reported that his staff could not find "any evidence showing the updated opioids [ADF opioids] actually reduce rates of addiction, overdoses, or death." [143]

520. In 2015, claiming a need to further assess its data, Purdue abruptly withdrew a supplemental new drug application related to reformulated OxyContin one day before FDA staff was to release its assessment of the application. The staff review preceded an FDA advisory committee meeting related to new studies by Purdue "evaluating the misuse and/or abuse of reformulated OxyContin" and whether those studies "have demonstrated that the reformulated

[142] CDC Guideline at 22 (emphasis added).
[143] Matthew Perrone, *Drugmakers Push Profitable, but Unproven, Opioid Solution*, AP (Jan. 2, 2017), https://www.publicintegrity.org/2016/12/15/20544/drugmakers-push-profitable-unproven-opioid-solution.